

ABSTRACT

The present invention relates to a modified enzyme of a non-heme iron (II) dependent family of oxygenases and oxidases which renders the enzyme dependent on bicarbonate for activity. In a preferred embodiment, the modification is an arginine, lysine, or other amino acid that is two amino acid residues upstream of a histidine residue that is an iron ligand in the enzyme and is one of the histidine residues of the 2-histidine-1-aspartic acid trifacial motif. In particular, the modified enzymes are isopenicillin N synthetase, deacetoxycephalosporin C synthetase, and deacetoxycephalosporin C synthetase/deacetylcephalosporin C synthetase which are used to make antibiotics. The present invention further provides a method for making antibiotics using a modified enzyme such as isopenicillin N synthetase, deacetoxycephalosporin C synthetase, and deacetoxycephalosporin C synthetase/deacetylcephalosporin C synthetase wherein the modification renders the enzyme dependent on bicarbonate for activity. Finally, the present invention provides a method for making antibiotics by providing the modified enzyme either in either an organism or in a cell-free system.